REVIEW

NIIGATA MINAMATA DISEASE: A REVISIT

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ABSTRACT

Minamata disease is a well-known mercury contamination that happened in Japan in 1953. Due to demand during world war, second mercury disaster occurred in Niigata Prefecture in 1965. This is a review on the Niigata Minamata disease based on available documents and local expert opinions on the disaster. The aims of this paper are to record exposure history like the source of mercury in Agano River and specific fish that was associated with the disease. It is for an appraisal of the basic mercury exposure control, particularly to protect Japanese and world population during that time. There was indication that initial exposure limit for mercury was calculated incorrectly, and higher safe dose was applied. This epidemiological study is very useful and significant in comprehend the correct estimation of the human exposure to any hazardous substances.

INTRODUCTION

Japan is one of the most developed countries in Asia's region. Its economy regained rapidly after the World War II[1]. Unfortunately, due to rampant progression, at least four incidents of environmental pollution occurred in this country[2]. The first catastrophe took place at the Minamata Bay in Kumamoto Prefecture, Japan in 1953. It is known as the Chisso-Minamata disease named after the factory that released organic mercury and contaminated all fishes. Neurological problems were the essential illnesses among the affected fishermen and their family[3-7]. A study on the leftover tissue of the historical cat's experiment fed with the factory wastewater in 1959, disclosed of high level of methyl mercury in cerebrum, cerebellum, kidney and liver[8].

Mercury poisoning in Niigata Prefecture is the fourth disaster after Itai-itai disease in Toyoma Prefecture in 1955[9,10] and Yokkaichi asthma in Mie Prefecture between 1960 and 1972[11]. It occurred in the Agano river basin with the first case noted in May 1965. And by July 1965, 26 patients have been identified, of which five of them already perished. Untreated wastewater of Showa Denso factory was identified as the source for high level of methyl mercury contamination in the river. The condition worsened when they started to increase their production rate due to higher demand after Chisso factory reduced its output. It has been 46 years since the first case of Niigata Minamata-disease was confirmed and yet hundreds of patients are still alive with neurological problems like tinnitus and numbness in their limbs for decades.

This paper is aimed to re-examine the initial protocol used in calculating mercury health risk and intended for documentation of a few facts that are currently being recorded only in the Japanese language.

Uses of Mercury in Japan Industries

During the Second World War, mercury was produced massively from plastic industries as a by-product of chemical reaction in acetaldehyde synthesis. Acetaldehyde is used as intermediate agents for acetic acid production, an important precursor in many manufacturer industries that produce bottle, cup and plate, cigarette filter, synthetic fibres and fabrics for Japanese Army Forces use. In the process, a carbon molecule from a carbide compound has to be extracted out by binding it with mercury molecules, which produces methyl mercury (Figure 1).

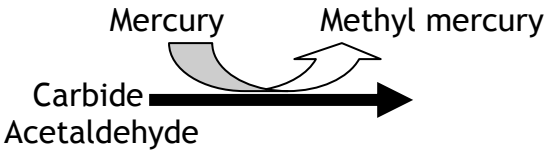

Figure 1. Methyl mercury as by-product

Methyl mercury (CH_3Hg^+) is known as a potent neurotoxin to humans and animals. The conversion from the elementary compounds to methyl mercury is a very complex biogeochemical process. It involves oxidation of inorganic mercury through a process named biomethylation. The process is primarily regulated by sulphate - reducing bacteria that prefer conditions of low dissolved oxygen (anoxic) like in water bodies and soils that happened in the Agano River.

The process rate is controlled by water temperature, salinity and acidity; sulphur content, dissolved organic carbon (DOC) and oxygen. However, main factors identified to influence the biomethylation process are DOC, stream flow of the river and wetland density of the basins[12]. The exposure is through fishes and shellfishes that ingested methyl mercury.

Niigata Prefecture

The prefecture is located on the Honshu Island. Its coastline stretches about 240km along the Japan Sea. Niigata is an agricultural state compromising of 10 districts with the total population of 2.5 million people. The fertile land of Niigata is irrigated by two main rivers, Shinano and Agano River. Shinano River, 367 kilometres, the longest river in Japan originates from Nagano. Agano River is the second longest river in this prefecture.

After the World War I, Niigata Prefecture has become the most important Japanese port city which was more industrialised and technically advanced than other cities in the region. Many camps were built for prisoners of war (POW) in Niigata Prefecture during the World War II mostly near to heavy industries areas. All prisoners were used as force labourers for the companies.

Kanose village is one of the locations for the camp known as Camp 16B. It was constructed in April 1944 side-by-side with establishment of the Showa Denso Plant. The Corporation used the POW labour force for its carbide production and coal mining. The plant was known as one of the main industries producing acetaldehyde in Japan.

Agano River was used as their main method of transportation and disposal of its wastewater. The river originates from the Mount Arakai, and flows down through the Fukushima Prefecture and ends near to the Niigata City. It has total length of 210km with 7,710km square watershed. As the main river used in agricultural activities in Niigata, it also plays many other roles. It serves an important part in cultivated irrigation (vegetables and paddy fields) and flood control since 160 years ago.

Agano River is also one of the main sources of protein, especially for the local people in the few fishermen villages along its river bank. The river is one of the important places for salmon hibernation. It's very rich in other fresh water life like crab, prawn and clam. In the past, it was one of the favourite locations for children to swim and play in water (Photo 1).

Photo 1. Children playing in the river

Niigata Minamata Disease

During the onset of the disease on 1st June 1965, nine local people were affected when two of them succumbed. Japanese government believed it was thallium poisoning through fishes ingestion. Professor Tadau Tsubaki of Niigata University was the first physician who examined those patients and diagnosed them as mercurialism due to their high mercury hair content to a maximum point of 390ppm. On 12th June 1965, he made a public statement about the poisoning. The government declared prohibition of fresh water fishing activity on 28th June 1965.

Another group of scientists led by Kitamura S. detected a high elevated content of mercury in all patients' hair and in particular, fishes consumed by them. Fishes like *Hemibarbus spp*, and *Tribolodon hakonensis* eel-like fish (Photo 2) were found to have very high of mercury content. The eel-like fish found to ingest plankton known as Datum (Photo 3) that bioaccumulate methyl mercury compound in it tissue.

Photo 2. Eel-like fishes hang dried for daily consumption.

Photo 3. Plankton (Datum) that bioaccumulate methyl mercury.

By end of 1965, 26 adults and five infants were diagnosed as Niigata Minamata disease patients. Later, they found a very high mercury concentration in the Showa Denso wastewater, the source of contamination released into the Agano River, about 160km upstream.

Tsubaki has documented his findings, of those patients, in which their signs and symptoms were similar to the Minamata disease sufferer in one of his papers titled 'Organic mercury intoxication in the Agano river area studied by Niigata University research group'. These findings were published in *Rinsho Shinkeigaku* (Journal of Clinical Neurology) Volume 8 in Japanese language in 1968.

Majority of the affected persons showed neurological symptoms, and their children had congenital malformations[13]. The obvious

differences between Minamata disease and Niigata Minamata disease was the prominent presence of Infant Minamata disease in Niigata Prefecture. Developing brains were affected by mercury through transplacental exposure and even by breastfeeding. More than 1500 infants became disabled with the first case in June 1967. They presented with neurological disability at the age of six months (Table 1). There was no treatment or medicine except to undergo physiotherapy.

Table 1. Signs among the affected children

Signs	Percentage
Mental retardation	100
Present of primitive reflexes	100
Coordination disturbance	100
Dysarthria	100
Limb deformation	100
Growth disorder	100
Choreoathetosis	95
Hypersalivation	95

Most of the disabled infants died of pneumonia, probably aspirated type due to swallowing problem. During recent reassessment for Niigata Minamata disease, a total of 30 autopsy cases were re-examined. Those patients were found to suffer of peripheral nerve lesions with formation of multiple vacuoles in their cerebellum cortex[5]. In 2010, a total of 696 patients have been recognized by local court as Niigata Minamata disease patients while another 700 people are still waiting for the endorsement.

The maximum level of methyl mercury detected in the Agano River water was 116 ppm (part per million) in August, 1966. After a massive soil removal and environmental cleaning, in April, 1978, the river was declared safe by the government. Later, during regular monitoring, the mean mercury concentration was documented as 0.155ppm (minimum of 0.019ppm and maximum of 0.620ppm) in 1989 and further decreased but slowly to 0.146ppm (minimum of 0.015ppm and maximum of 0.340ppm) in 1997[14].

Calculation the Acceptable Daily Intake (ADI)

A local scientist named Kojima and his colleges have examined 735 patients of Niigata Minamata disease. They detected the concentration of hair mercury in those patients ranged from 57 to 570ppm. Based on that, they decided to take the hair concentration of mercury at 50ppm as a safe threshold level. It was based on assumption that the concentration of lesser than 57ppm hair mercury will not produce the disease. Therefore, 50ppm concentration was predicted not to pose any health problem and accepted as the non-observed adverse effect level (NOAEL) at that time. Later, he derived a formula between the mercury concentration in hair sample and mercury consumption based on linear association between both factors:

Equation 1:

$Y = 150X + 1.66$

Y = mercury concentration in hair (ppm)

X = mercury intake (mg/person/day)

Using the equation, he calculated the value of 0.32mg/person/day or 320µg/person/day as a risk-free daily mercury intake. For safety reasons, he further used an uncertainty factor of 10 to derive the safe daily mercury intake per person:

$$\frac{320\mu g/person/day}{10} = 32\mu g/person/day$$

Using an average of Japanese body weight of 50 kg, he obtained the acceptable daily intake (ADI) of 0.64µg/kg/day, which was higher than the United States Environmental Protection Agency (USEPA) guideline of

0.37μg/kg/day based on the World Health Organisation findings. Thus in June 1973, the Japanese Ministry of Health and Welfare set a lower provisional limit of methyl mercury intake of 0.48μg/kg/day or 24μg/person/day, which was still excessive.

For a 50kg body weight Japanese people, Kojima derived the ADI of 0.44μg/kg/day, which was higher compared to USEPA limit (0.37μg/kg/day). As one of the high fish consumption countries, he suggested for a limited consumption of only 108.9g/day for everyone in Japan. If he used the correct method of risk calculation, the total amount of fish intake would be further reduced.

DISCUSSION

There were few differences or mistakes that occurred unintentionally during the initial mercury risk intake calculation by the Japanese scientist. First, there was a vast contradiction of hair mercury concentrations done by both local and WHO researcher groups. WHO researchers had detected that one patient had hair mercury concentration as low as 50ppm. The maximum concentration detected was as high as 1000ppm, instead of 570ppm by local scientist.

Second point, the hair mercury concentration of 50ppm had a potential to be the lowest observable adverse effect level (LOAEL) instead of NOAEL as postulated by Kojima. In addition, he also didn't divide the hair mercury concentration first before incorporating it into the equation that gave rise to five ppm as the high 'safe threshold' at that time. The limit set by him (0.32mg/person/day) was approximately one and half higher than the correct limit (0.22mg/person/day).

As the third concern, the levels above were based on mercury concentration in hair among Niigata patients where most of them were adults and children. It was suitable only for acute and severe exposures[15], but not for chronic exposures as it happened among those pregnant mothers and their foetus in Niigata. Based on those issues, USEPA did a review on the oral reference dose (RfD) and lowered the level to 0.1μg/kg/day[16]. It was based on two large prospective epidemiology studies in the Seychelles Islands[17], and the Faroe Islands, which were designed to protect childhood development and neurotoxicity in relation to foetal exposures.

The fourth argument is on the average exposure to methyl mercury from marine fish, which is 0.027ug/kg/day[16]. This exposure represents almost 30% of the RfD, which does not include air, water, non fish dietary food and soil sources. Japan takes 0.50ug/kg/day as their allowable exposure to methyl mercury but only from marine sources. By adding another 70% from other sources, people of Japan might be exposed to an extra for 1.2ug/kg/day. For average people with 60kg body weight, he/she exposed to 72ug/person/day, which was double than the safe level by Kojima, and triple to USEPA limit.

The last concern is that the people in the area might still be exposed to chronic mercury poisoning present in other sources of food-chain along the Agano River. For example, they also found high mercury content in their paddy field which was three times higher compared to other uncultivated soil around it. The presence of crops and vegetarian might attract mercury accumulation in certain type of soil.

CONCLUSION

This paper documented a few facts and misjudgements that occurred during the initial risk assessment of mercury poisoning by the local scientists. It led

to an unacceptable daily intake limit which may cause various neurobehavioural or chronic kidney problems among the people. A true level of mercury concentration in the affected food chain needs to be reassessed before the accurate health risk can be determined. Even without any further contamination by Showa-Denso Company, the possibility of mercury contamination from other sources like pesticide might exist. Thus, the possibly of the people in the affected area being exposed to a higher level of mercury intake is undoubted.

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REFERENCES

1. Thomas Piketty and Emmanuel Saez. The Evolution of Top Incomes: A Historical and International Perspective. *The American Economic Review* 2006; **96** (2): 200-205.

2. Katsumi Yoshida, Kunimasa Morio and Kazuhito Yokoyama. Epidemiology and Environmental Pollution: A Lesson from Yokkaichi Asthma, Japan. *Progress in Environmental Research* 2007: 263–278.

3. Eto K. Pathology of Minamata disease. *Toxicological Pathology* 1997; **25**(6): 614-623.

4. Eto K. Minamata Disease. *Neuropathology* 2000; (20) Supplement: S14-19.

5. Eto K, Tokunaga H, Nagashima K, Takeuchi T. An autopsy case of Minamata disease (methyl mercury poisoning); pathological viewpoints of peripheral nerves. *Toxicological Pathology* 2002; **30**(6):714-722.

6. Yorifuji T, Tsuda T, Takao S, Suzuki E, Harada M. Total mercury content in hair and neurologic signs: historic data from Minamata. *Epidemiology* 2009; **20**(2):188-193.

7. Ekino S, Susa M, Ninomiya T, Imamura K, Kitamura T. Minamata disease revisited: an update on the acute and chronic manifestations of methyl mercury poisoning. *Journal of the Neurological Sciences* 2007; **262**(1-2):131-144.

8. Eto K, Yasutake A, Nakano A, Akagi H, Tokunaga H, Kojima T. Reappraisal of the historic 1959 cat experiment in Minamata by the Chisso Factory. Tohoku *Journal of Experimental Medicine* 2001; **194**(4):197-203.

9. Mirei Uetani, Etsuko Kobayashi, Yasushi Suwazono, Ryumon Honda, Muneko Nishijo, Hideaki Nakagawa, Teruhiko Kido and Koji Nogawa. Tissue cadmium (Cd) concentrations of people living in a Cd polluted area, *Japan. Biometals* 2006; **19**(5):521-525.

10. Etsuko Kobayashi, Yasushi Suwazono, Mirei Dochi, Ryumon Honda and Teruhiko Kido.

Influence of Consumption of Cadmium-Polluted Rice or Jinzu River Water on Occurrence of Renal Tubular Dysfunction and/or Itai-itai Disease. *Biological Trace Element Research* 2008; **127** (3):257-268.

11. Peng Guo, Kazuhito Yokoyama, Masami Suenaga and Hirotaka Kida. Mortality and life expectancy of Yokkaichi Asthma patients, Japan: Late effects of air pollution in 1960–70s. *Environmental Health* 2008: 7–8.

12. Mark E. Brigham, Dennis A. Wentz, George R. Aiken and David P. Krabbenhoft. Mercury Cycling in Stream Ecosystems. 1. Water Column Chemistry and Transport. *Environmental Science & Technology* 2009; **43** (8): 2720 – 2725.

13. Kondo K. Congenital Minamata disease: warnings from Japan's experience. *Journal of Children Neurology* 2000; **15**(7):458-464.

14. Ryozo Nakagawa & Yukie Yumita. Change and behavior of residual mercury in paddy soils and rice of Japan. *Chemosphere* 1998; **37** (8): 1483-1487.

15. Yorifuji T, Tsuda T, Takao S, Harada M. Long-term exposure to methylmercury and neurologic signs in Minamata and neighbouring communities. *Epidemiology* 2008; **19**(1): 3-9.

16. USEPA. Water Quality Criterion for the Protection of Human Health: Methyl-mercury. Office of Science and Technology Office of Water. U.S. Environmental Protection Agency. Washington. 2001. EPA-823-R-01-001.

17. Crump KS, Van Landingham C, Shamlaye C, Cox C, Davidson PW, Myers GJ, Clarkson TW. Benchmark concentrations for methylmercury obtained from the Seychelles Child Development Study. *Environmental Health Perspectives* 2000; **108**(3):257-63.